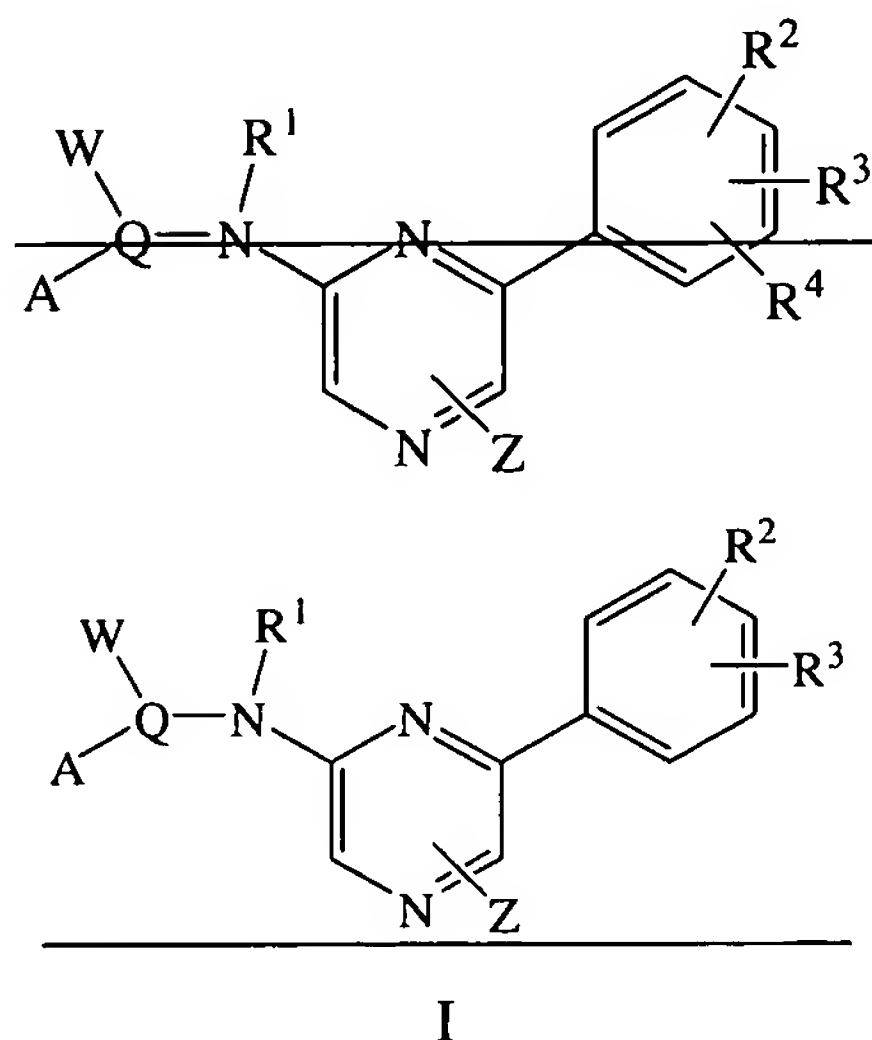


CLAIM AMENDMENTS

1. (currently amended): ~~A compound~~ tubulin inhibitor of the formula [[I]]

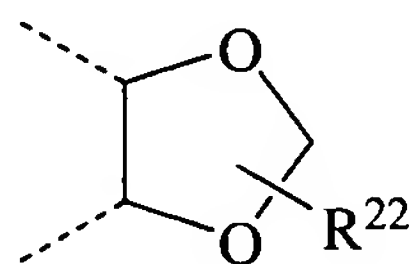


~~or pharmaceutically acceptable prodrugs, salts or stereoisomers thereof, wherein:~~

R^1 is H, C_{1-6} alkyl, C_{1-6} alkyl NR^5R^6 , C_{1-6} alkyl NR^5COR^6 , C_{1-6} alkyl $NR^5SO_2R^6$, C_{1-6} alkyl CO_2R^5 , C_{1-6} alkyl $CONR^5R^6$, where R^5 and R^6 are each independently H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkylaryl, C_{1-4} alkylhetaryl or may be joined to form a 3-8 membered ring optionally containing an atom selected from O, S, NR^7 and R^7 is selected from H, C_{1-4} alkyl;

R^2 [[,]] and R^3 ~~and~~ R^4 are each independently [[H,]] halogen, C_{1-4} alkyl, OH, OC_{1-4} alkyl, CF_3 , OCF_3 , CN, C_{1-4} alkyl NR^8R^9 , OC_{1-4} alkyl NR^8R^9 , $CONR^8R^9$, NR^8R^9 , NR^8COR^9 , $NR^{10}CONR^8R^9$, $NR^8SO_2R^9$, $COOR^8$, $CONR^8R^9$; [[and]] wherein R^8 , R^9 and R^{10} are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cycloalkyl, or may be joined to form a 3-8 membered ring optionally containing an atom selected from O, S, NR^{11} ; wherein R^{11} is H, C_{1-11} alkyl or CF_3 ;

alternatively, ~~two of~~ R^2 [[,]] and R^3 ~~and~~ R^4 , when located on adjacent carbon atoms, may be joined to form the ring system



where R^{22} is H, C_{1-4} alkyl, or CF_3 ;

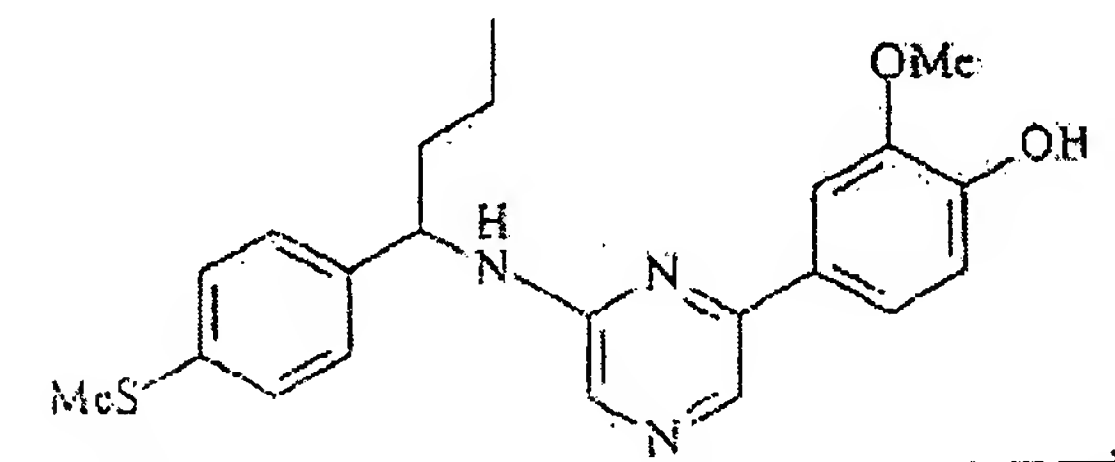
Q is C₁₋₄ alkylene;

W is ~~selected from~~ C₂₋₄alkyl or C₂₋₆alkenyl, where C₂₋₄alkyl or C₂₋₆alkenyl may be optionally substituted with C₁₋₄ alkyl, OH, OC₁₋₄ alkyl, NR¹⁵R¹⁶; [[and]] wherein R¹⁵, and R¹⁶ are each independently H, C₁₋₄ alkyl, C₁₋₄ alkyl cycloalkyl, C₁₋₄ alkyl cyclohetalkyl, aryl, hetaryl, or may be joined to form a 3-8 membered ring optionally containing an atom selected from O, S, NR¹⁷ [[and]] wherein R¹⁷ is selected from H[[,]] or C₁₋₄ alkyl;

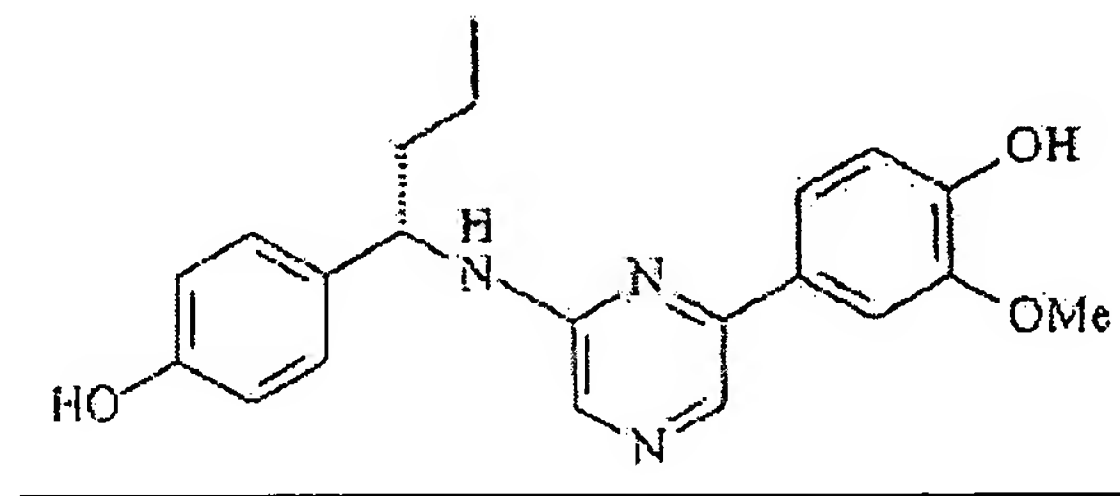
A is aryl, or hetaryl each optionally substituted with 0-3 substituents independently selected from halogen, C₁₋₄ alkyl, CF₃, aryl, hetaryl, OCF₃, OC₁₋₄ alkyl, OC₂₋₅ alkylNR¹⁸R¹⁹, Oaryl, Ohetaryl, CO₂R¹⁸, CONR¹⁸R¹⁹, NR¹⁸R¹⁹, C₁₋₄ alkylNR¹⁸R¹⁹, NR²⁰C₁₋₄ alkylNR¹⁸R¹⁹, NR¹⁸COR¹⁹, NR²⁰CONR¹⁸R¹⁹, NR¹⁸SO₂R¹⁹; [[and]] wherein R¹⁸, R¹⁹ are each independently H, C₁₋₄ alkyl, C₁₋₄ alkyl cyclohetalkyl, aryl, hetaryl, C₁₋₄ alkyl aryl, C₁₋₄ alkyl hetaryl, or may be joined to form a 3-8 membered ring optionally containing an atom selected from O, S, NR²¹; [[and]] wherein R²⁰ is selected from H, C₁₋₄ alkyl; and R²¹ are independently is selected from H[[,]] or C₁₋₄ alkyl; and

Z is H or C₁₋₄ alkyl,

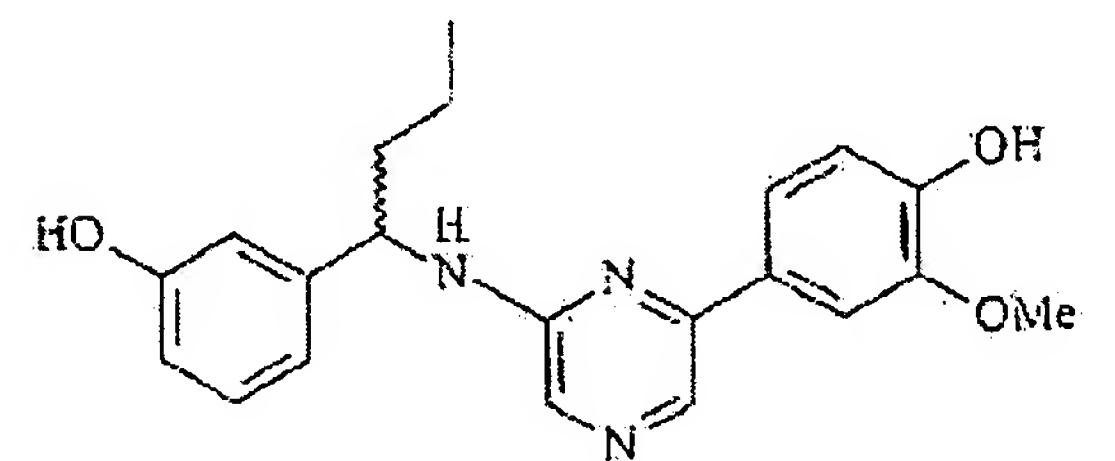
or a tubulin inhibitor of the formula



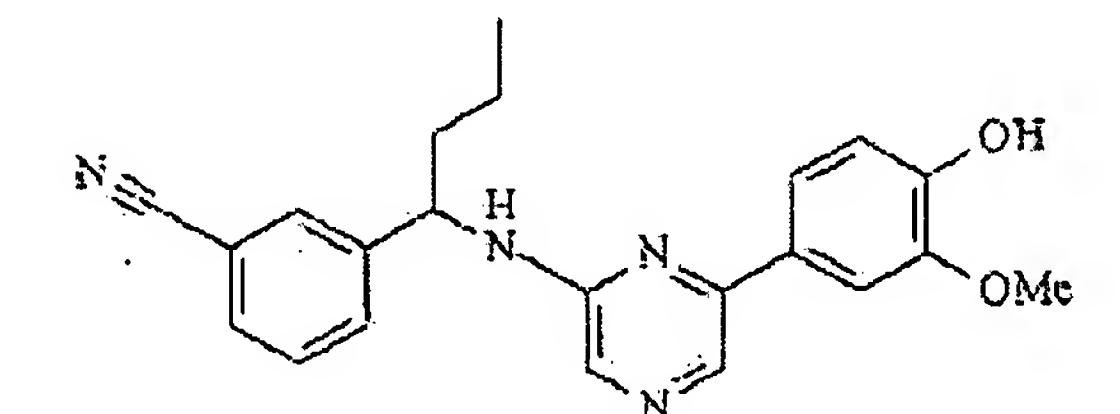
1-1



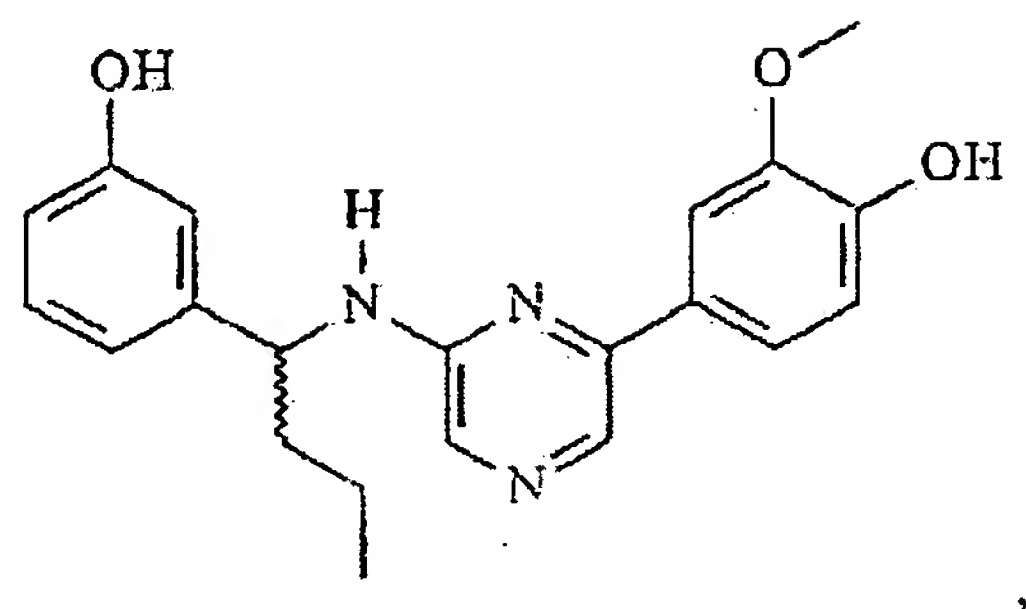
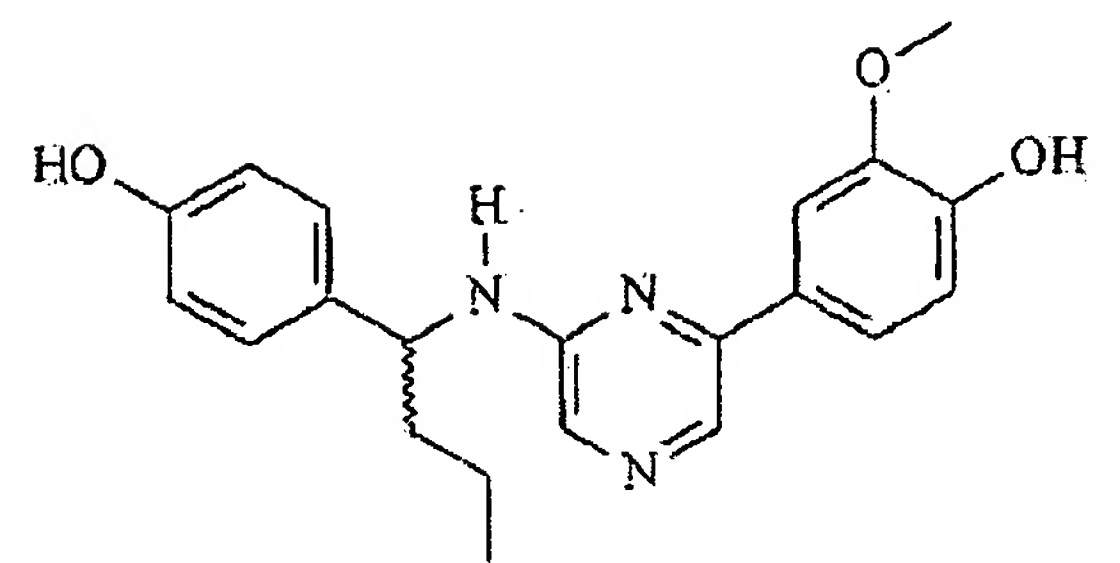
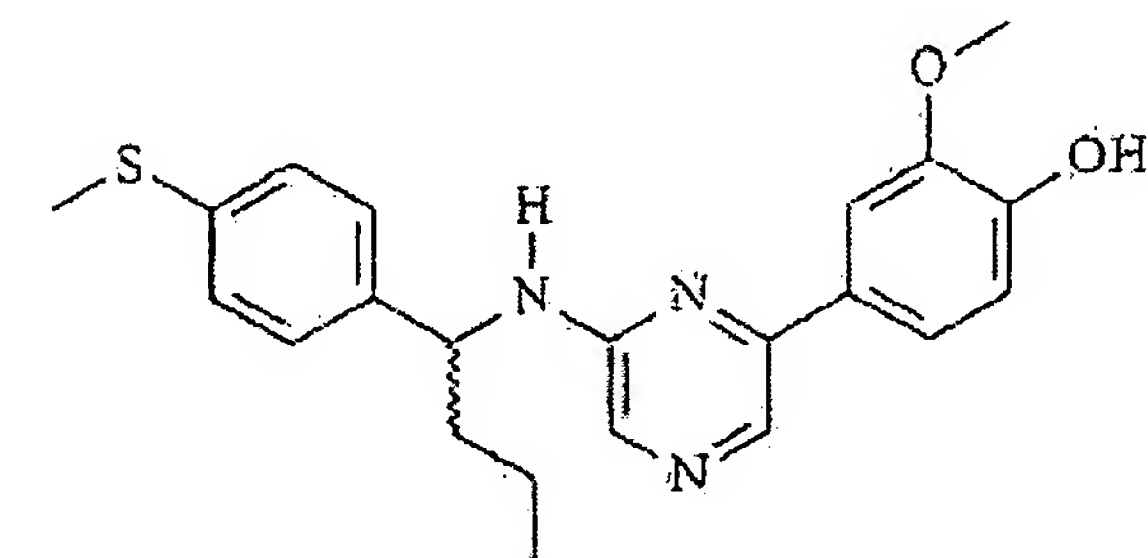
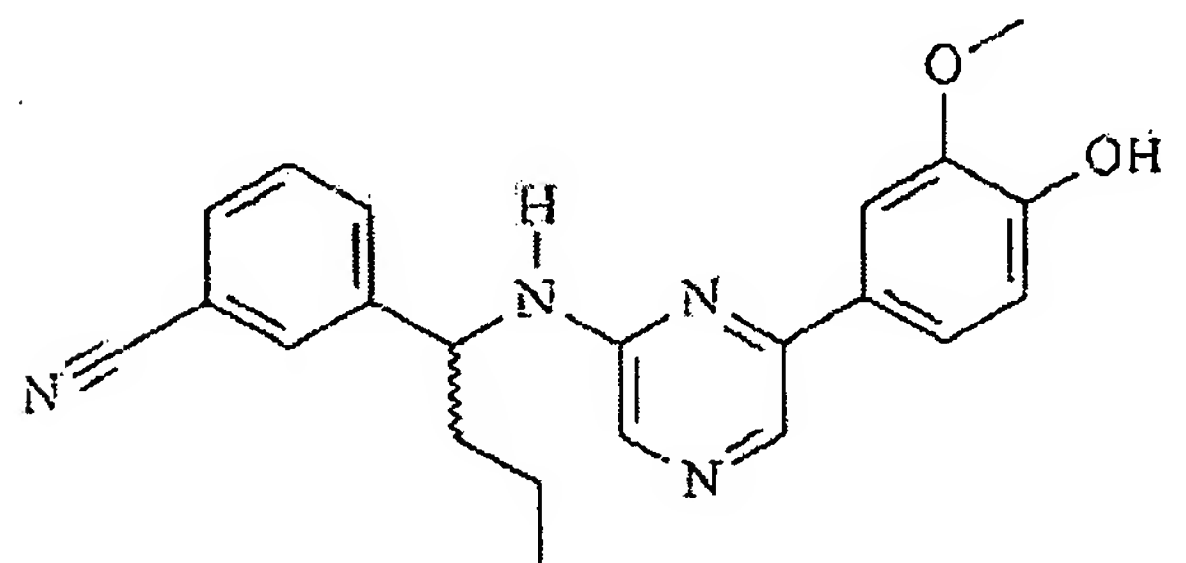
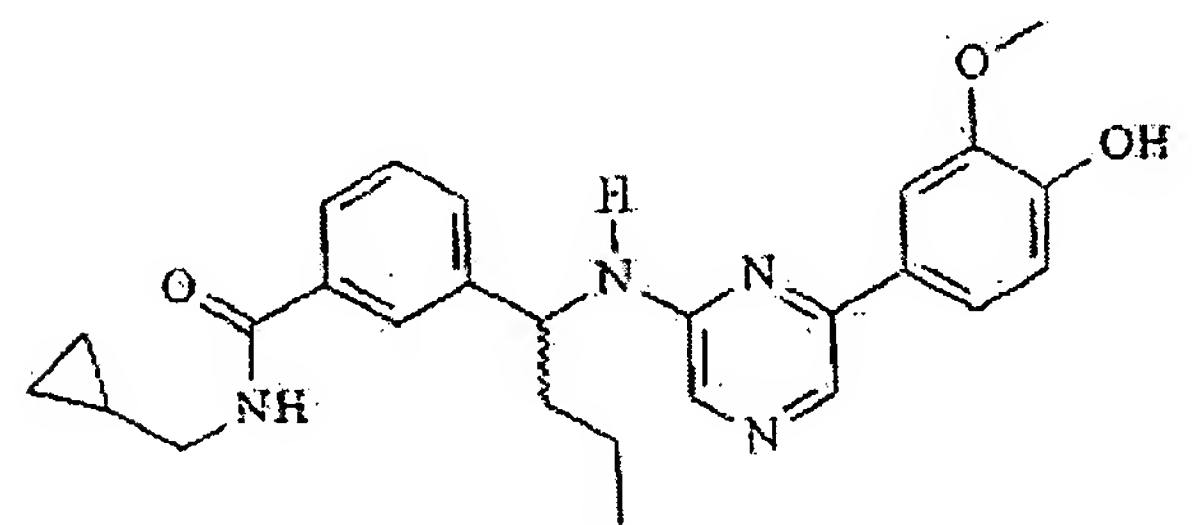
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1-3



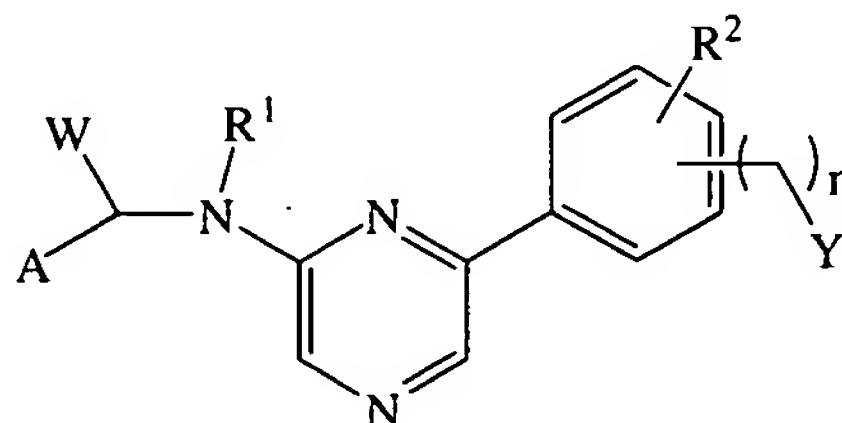
1-4

1-51-61-71-81-9

or pharmaceutically acceptable prodrugs, salts or stereoisomers thereof,

wherein said prodrugs are esters of a free carboxyl or hydroxyl group or amides of a free amino group.

2. (currently amended): A ~~compound~~ tubulin inhibitor of the formula [[II:]]



II

or pharmaceutically acceptable prodrugs, salts or stereoisomers thereof, wherein:

R^1 is H, C_{1-6} alkyl, C_{1-6} alkylNR⁵R⁶, where R⁵ and R⁶ are each independently H[,] or C_{1-4} alkyl, or may be joined to form a 3-8 membered ring optionally containing an atom selected from O, S, NR⁷ ~~[[and]]~~ wherein R⁷ is ~~selected from~~ H[,] or C_{1-4} alkyl;

A is aryl, or hetaryl each optionally substituted with 0-3 substituents independently selected from halogen, C_{1-4} alkyl, CF₃, aryl, hetaryl, OCF₃, OC₁₋₄alkyl, OC₂₋₅alkylNR¹⁸R¹⁹, Oaryl, Ohetaryl, CO₂R¹⁸, CONR¹⁸R¹⁹, NR¹⁸R¹⁹, C_{1-4} alkylNR¹⁸R¹⁹, NR²⁰ C_{1-4} alkylNR¹⁸R¹⁹, NR¹⁸COR¹⁹, NR²⁰CONR¹⁸R¹⁹, NR¹⁸SO₂R¹⁹, where R¹⁸, R¹⁹ are each independently H, C_{1-4} alkyl, C_{1-4} alkylcyclohetalkyl, aryl, hetaryl, C_{1-4} alkylaryl, C_{1-4} alkylhetaryl, or may be joined to form a 3-8 membered ring optionally containing an atom selected from O, S, NR²¹; R²⁰ is ~~selected from~~ H[,] or C_{1-4} alkyl; ~~[[and]]~~ wherein R²¹ is ~~selected from~~ H or C_{1-4} alkyl;

R² is ~~[[0-2]]~~ 1-2 substituents independently selected from halogen, C_{1-4} alkyl, OH, OC₁₋₄ alkyl, CF₃, OCF₃, CN, C_{1-4} alkylNR⁸R⁹, OC₁₋₄ alkylNR⁸R⁹, CO₂R⁸, CONR⁸R⁹, NR⁸R⁹, NR⁸COR⁹, NR¹⁰CONR⁸R⁹, NR⁸SO₂R⁹; ~~[[and]]~~ wherein R⁸, R⁹ and R¹⁰ are each independently H[,] or C_{1-4} alkyl;

Y is H, OH, NR¹²R¹³; and R¹², ~~[[and]]~~ wherein R¹³ are each independently H[,] or C_{1-4} alkyl, or may be joined to form a 3-6 membered ring optionally containing an atom selected from O, S, NR¹⁴ ~~[[and]]~~ wherein R¹⁴ is ~~selected from~~ H[,] or C_{1-4} alkyl;

n is 0, 1, 2, 3 or 4;

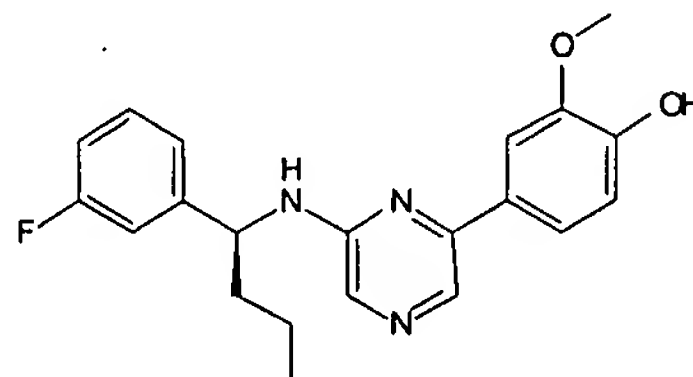
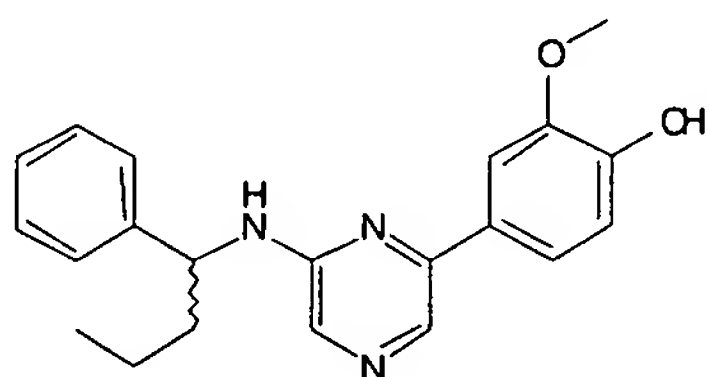
with the proviso that if R² represents 2 substituents, n is 0 and Y is H; and

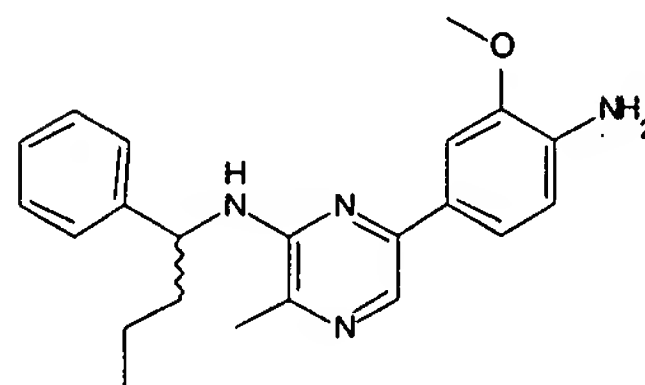
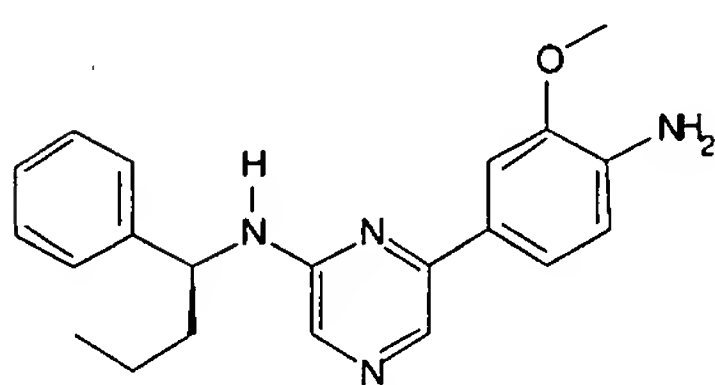
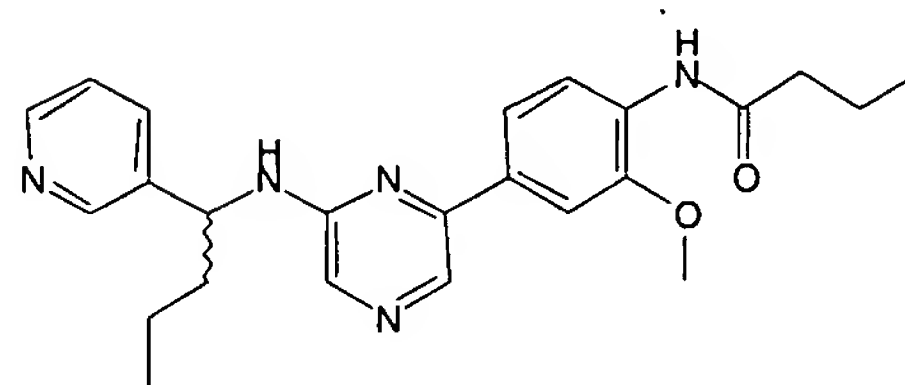
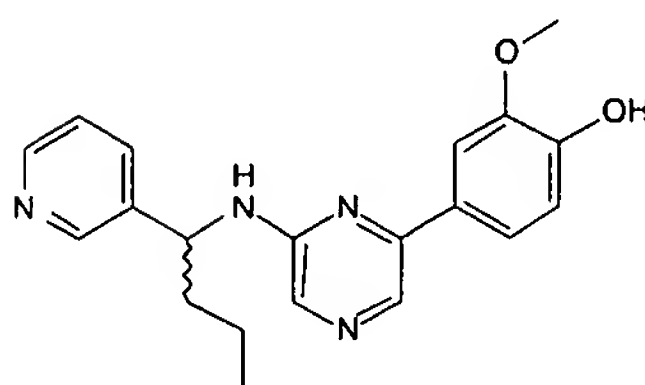
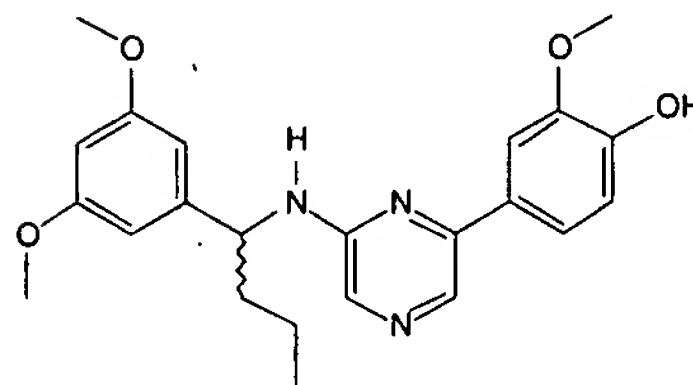
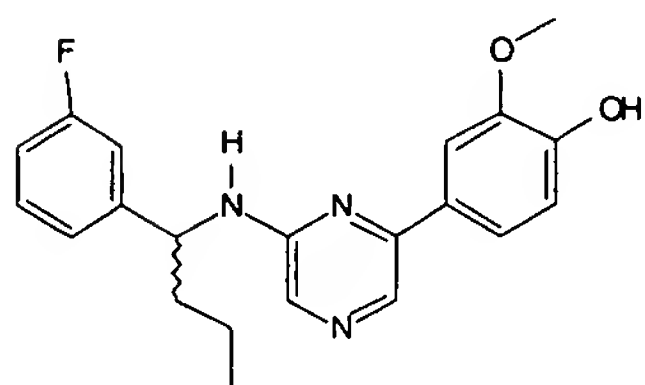
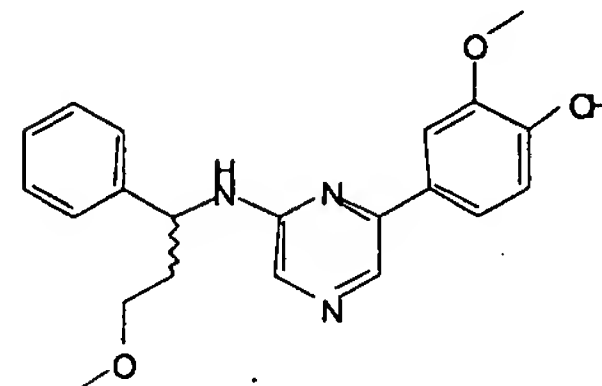
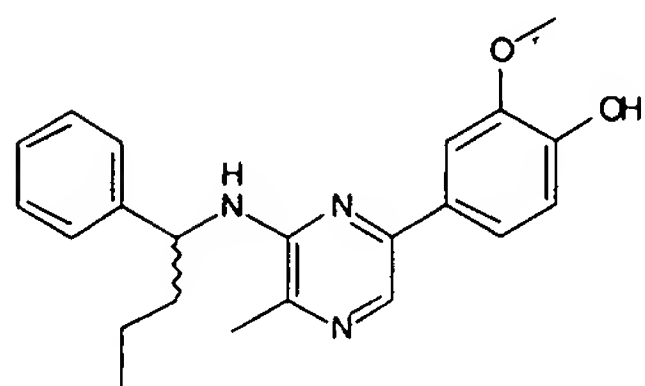
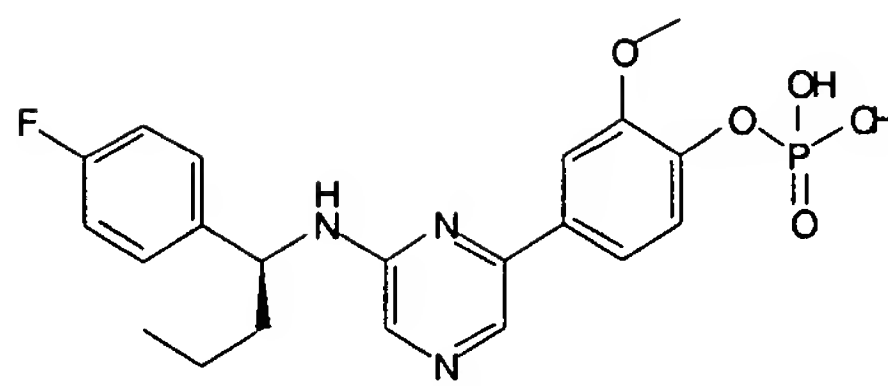
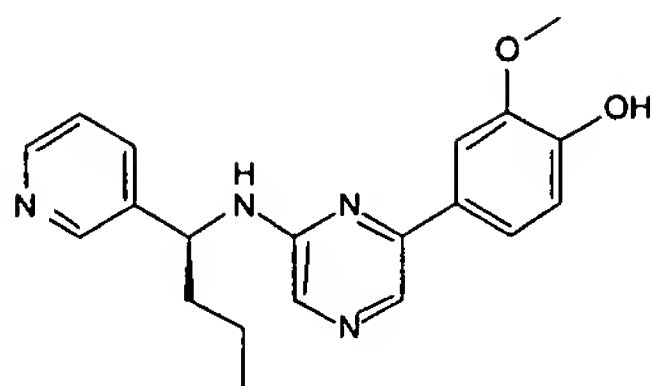
if R² represents one substituent and n is 0, Y cannot be H;

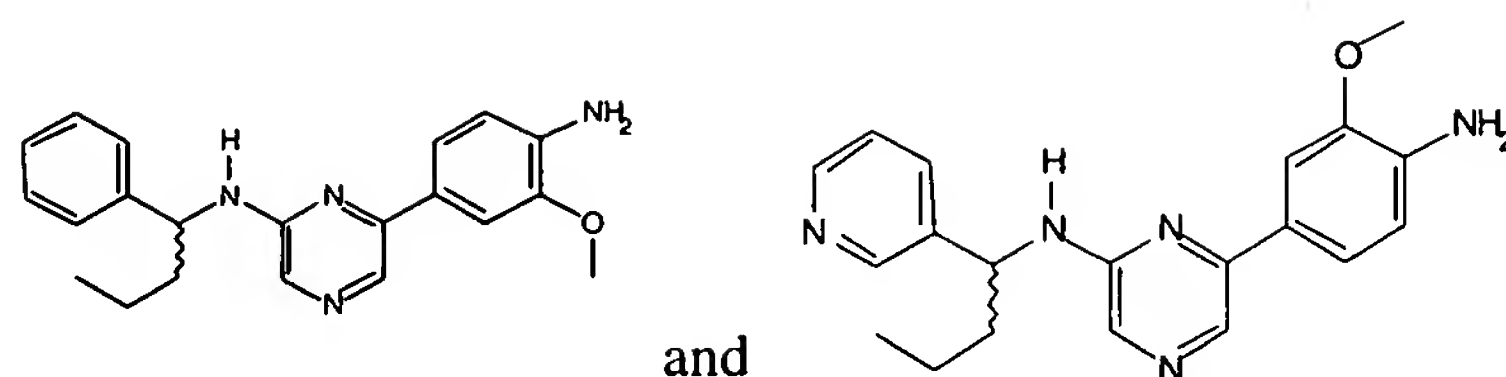
W is ~~selected from~~ C_{2-4} alkyl or C_{2-6} alkenyl, where C_{2-4} alkyl or C_{2-6} alkenyl may be optionally substituted with C_{1-4} alkyl, OH, OC₁₋₄ alkyl, NR¹⁵R¹⁶; ~~[[and]]~~ wherein R¹⁵ and R¹⁶ are each independently H, C_{1-4} alkyl, C_{1-4} alkylcycloalkyl, C_{1-4} alkylcyclohetalkyl, aryl or hetaryl, or may be joined to form a 3-8 membered ring optionally containing an atom selected from O, S or NR¹⁷; ~~[[and]]~~ wherein R¹⁷ is selected from H or C_{1-4} alkyl; ~~[[and]]~~

wherein prodrugs are esters of a free carboxyl or hydroxy group or amides of a free amino group.

3. (currently amended): ~~A compound~~ tubulin inhibitor according to claim 1 wherein W is C₂₋₄alkyl or C₂₋₄alkylamino which is a mixture of the compound that possesses S chirality at the chiral carbon bearing W, and the compound that possesses R chirality at said carbon.
4. (currently amended): ~~A compound~~ tubulin inhibitor according to claim 3 wherein the mixture comprises at least 70% of the compound that possesses S chirality at said carbon.
5. (currently amended): ~~A compound~~ tubulin inhibitor according to claim 4 wherein the compound comprises at least 80% of the compound that possesses S chirality at said carbon.
6. (currently amended): ~~A compound~~ tubulin inhibitor according to claim 4 wherein the compound comprises at least 90% of the compound that possesses S chirality at said carbon.
7. (currently amended): ~~A compound~~ tubulin inhibitor according to claim 4 wherein the compound comprises at least 95% of the compound that possesses S chirality at said carbon.
8. (currently amended): ~~A compound~~ tubulin inhibitor according to claim 4 wherein the compound comprises at least 99% of the compound that possesses S chirality at said carbon.
9. (currently amended): ~~A compound~~ tubulin inhibitor selected from the group consisting of:







and the pharmaceutically acceptable salts and stereoisomers thereof.

10. (currently amended): A composition comprising a carrier and at least one ~~compound~~ tubulin inhibitor of claim 1.

11-14. (canceled)

15. (currently amended): A method of modulating microtubule polymerization in a cell wherein said method comprises administering a ~~compound~~ tubulin inhibitor according to claim 1.

16. (currently amended): A method of modulating microtubule polymerization in a cell wherein said method comprises administering a ~~compound~~ tubulin inhibitor according to claim 2.

17. (canceled)

18. (new): A composition comprising a carrier and at least one tubulin inhibitor of claim 2.

19. (new): A composition comprising a carrier and at least one tubulin inhibitor of claim 9.

20. (new): A method of modulating microtubule polymerization in a cell wherein said method comprises administering a tubulin inhibitor according to claim 9.